APPENDIX A

CITY OF HOPE INVENTION DISCLOSURE FORM

This Invention Disclosure Form is an important legal document. Care should be taken in its preparation. In responding to the questions below, please provide sufficient information that will enable the Institution to evaluate the commercial potential of inventions or discoveries that you have made. If a decision is made to proceed with patent protection, your disclosure will be referred to patent counsel. Please limit your comments to factual information concerning your ideas and work and avoid opinions or comments concerning legal questions, such as patentability, inventorship, date of conception or reduction to practice and the like. Use additional sheets if necessary.

If you would like assistance, please contact the Office of Technology Development & Transfer at extension 63536.

Please submit the completed Form, with original signatures, directly to the Vice President, Office of Technology Development & Transfer.

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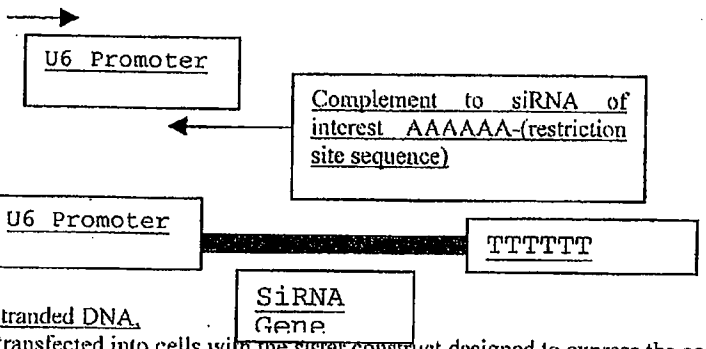
1. Short descriptive title of the invention.

A facile method for synthesis of siRNA encoding expression constructs.

2. Provide a brief summary of your research and ideas that you have for further related work that you believe may warrant patent protection. Please include a brief description of the practical utilities of your work and ideas and include a summary of the state of the art at the time of your work. If you have previously prepared a manuscript or other description of your work, please attach a copy.

SiRNA is a potent form of targeted transcript inactivation that appears to be present in most eukaryotic organisms. In mammalian cells, si RNAs (21-23 nt double stranded inhibitory RNAs) can be generated from longer double stranded transcripts, but the sequence specific effects are often lost due to the potent double stranded RNA activation of the Interferon and PKR inhibitory pathways. In a previous invention we have demonstrated that the use of a Pol III based promoter system can be used to effectively make the 21-23 base double stranded siRNAs in mammalian cells. This procedure involved cloning of siRNA encoding genes downstream of the human U6 snRNA Pol III promoter. The present invention disclosure depicts a rapid method for creating siRNA genes driven by U6, and may or may not required cloning of the genes in a vector. The products of this technique may be directly transfected into cells, thereby allowing rapid expression screening of siRNAs in mammalian cells.

The overall plan is to use PCR based gene synthesis with primers complementary to the U6 promoter. The upstream primer can have the sequence 5'AAGGTCGGGCAGGAAGAGGG 3', or some shorter or longer derivative thereof. If one wants to clone the gene, then appropriate restriction site sequences are added to the 5' end of the primer. The downstream primer has the following characteristics. 5'CGGTGTTTCGTCCTTTCCAC3' or some shorter or longer derivative. Attached to the 5' end are either a restriction site followed by 6 Adenosines, or six Adenosines. The Adenosines are followed by a 21 base sequence that is complementary to either the sense or antisense of the siRNAs to be made.



Since this is double stranded DNA,
It can be directly co-transfected into cells with the sister construct designed to express the complementary siRNA.
Alternatively, if restriction sites are added to the 5' and 3' primers, the genes can be cloned in an appropriate DNA vector system. The siRNAs will be transcribed from the U6 promoter, and will terminate within the string of U's encoded at the end of the message.

provided salary, research funds, equipment and/or facilities for the research described in this Invention Disclosure Form. If you are uncertain about funding or outside support, please consult with the Office of Sponsored Research or the Office of Technology Transfer prior to completing this section.

Funding Source/Sponsor*	Contract or Grant Number	Principal Investigator
NIH	AI29329	John Rossi

4. Were any materials used in the research described in this Invention Disclosure Form obtained from another source under a "Material Transfer Agreement" or other written understanding? If so, indicate the materials and their source(s).

No

5. Have you submitted or do you plan to submit a report, abstract, paper, or thesis relating to this invention for publication, for presentation at a conference, or to a research sponsor? YES_____ NO_x_____

If yes, give details, including date of submission or planned submission and whether a manuscript has been accepted. Append copy of document.

6. Identify any references, patents, patent applications or other publications of which you are aware relating to the research and ideas described in this Invention Disclosure Form. Please attach copies of these materials, if available. *You are not required to make a search of the prior art.*

My Own Applicagtion 1954-392

7. Provide, to the best of your knowledge, the names and addresses (if available) of companies that are or may be interested in manufacturing, using, and/or further developing your invention. (Optional Information)

RPI, Insert Therapeutics, Deltagen, Immusol, any of the large pharma, all of which are interested in siRNA technology

8. List those individuals who, individually or jointly, contributed intellectually to the research and ideas described in this Invention Disclosure Form. Please note that inventorship under the patent laws is a legal issue, and often the person(s) identified as inventors on a patent will be different from those who will be listed as authors on a scientific publication. In addition, inventorship is determined by reference to the patent claims that are submitted with the patent application and may change as claims are amended during prosecution of the patent application. Accordingly, patent counsel will determine the inventorship after considering pertinent information. The purpose of the following listing is to identify individuals from whom patent counsel may obtain relevant information.

9. Print Name: Daniela Castanotto Signature

Hm Address: 1941 E. BRAEBURN RD. [illegible] Citizenship:

Wk Address: [illegible]

Print Name: John J. Rossi Signature

Hm Address: [illegible] Citizenship: U.S.A.

Wk Address:

*Federal law requires certain disclosures to the funding agency of inventions made with U.S. government funding.

Print Name:_____ Signature_____

Hm Address:_____ Citizenship:_____

Wk Address:_____

Print Name:_____ Signature:_____

Hm Address:_____ Citizenship:_____

Wk Address:_____

10. Obtain the signatures of corroborating witnesses who are not inventors but are capable of understanding the subject matter described in this disclosure. The Office of Technology Development can provide one of these witnesses. I, the undersigned, have read and understand the material presented in this Invention Disclosure Form, and attest that I am not an inventor of the described invention.

_____ Date:_____

Larry A. Couture, Ph.D.
Senior Vice President for Technology Development & Transfer